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EXAMINER
HAQ, SHAFIQUL

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
01/14/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/533,950	ROGET ET AL.	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 10-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

1. Applicant's amendments and arguments filed 9/14/2009 is acknowledged and entered. Claims 1-6 and 10-29 are pending and examined on merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 26-29 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (New matter). The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 26, 27, 28 and 29 lack written descriptive support for the following recitations in the specification: "wherein the activity of the protein prior to attachment is conserver after its attachment to the conductive support" and "wherein the ability of the protein prior to attachment to be specifically recognized by an antibody is conserver after its attachment to the conductive support".

Specification does not disclose comparing activity of protein before and after attachment to conductive support and specification does not disclose comparing the ability of proteins to be specifically recognized by an antibody before and after attachment to conducting support. Further "conserved"

activity and "conserver" ability to be specifically recognized by an antibody have not been defined in the specification and 10%, 50% or 100% retained activity/ability after attachment to conductive support can be regarded to "conserved" activity/ability. Specification has not disclosed 100% retained activity/ability of a protein after attachment to solid support.

New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., In re Lukach, 442 F.2d967, 169 USPQ 795 (CCPA 1971).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 6, 10-21 and 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Guedon *et al* (Anal Chem. 2000).

Livache *et al* disclose a method of immobilization of biological material (e.g. peptides, protein. See the Title) (lines 14-15, right column of page 629) to a conductive support (e.g biochip) by means of a pyrrole polymer (see abstract and introduction). The method comprises coupling peptides to dT_{10} linked pyrrole monomer (i.e. an activated pyrrole monomer) (see section 2.1.

of page 630) to provide peptide pyrrole coupling compound and mixing solutions of pyrrole monomer (which is not coupled to peptide) and the peptide-pyrrole to obtain an electropolymerization solution and elctropolymerization to obtain a film of copolymer on conductive medium (see sections 2.1. and 2.3. of page 630). The pyrrole copolymerization process allows the preparation of addressed probes such as polypyrrole-DNA or equivalent polypyrrole-protein on blocks of biosensor array (see section 3.; fig.5 and lines 6-9, right column of page 633) for detection of DNA or other equivalent analyte such as proteins. Examples of immobilization of proteins (e.g. ACTH hormone) and DNA (Fig. 5; Fig.6 and section 3.4.) are also disclosed.

Livache et al disclose different thickness (from 2 to 80 nm approximately) which were obtained by applying an amount of current from 10 to 400uC/mm^2 (section 3.2., 3.4. and Fig. 4) but do not mention electopolymerization being carried out with a charge of less that 50uC/mm^2, for a synthesis time of less than 1000ms.

Guedon *et al* in a polypyrrole-based DNA sensor disclose six different thicknesses of polypyrroly-ODN spots made by performing the synthesis for 250ms to 1000ms leading to 9-14 nm thick films (page 6007, left column, left column, lines 3-12). The film synthesis is very fast taking about 500ms to spot an 11 nm thick film by a 2-V electrochemical pulse (page 6004, lines 30-31 of left column and page 6005, left column, lines 7-8). Goedon *et al* also disclose that for optimal hybridization signal, optimal thickness of the spot was found

to be close to 11 nm (see abstract; page 6007, lines 1-1-26 of left column and Fig. 6).

Therefore, given the above fact that a film of pyrrole containing copolymer having a thickness close to 11 nm is desirable for optimal hybridization signal (Guedon et al) in a pyrrole based DNA sensor, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to provide similar polymer film thickness close to 11nm (i.e 10nm) in the pyrrole based biosensor of Livache et al, with the expectation of enhancing detection signal with a reasonable expectation of success and to produce a thickness close to nm within 250ms to 1000ms (Goedon) with a electrode of 50um x 50um, an electric current of less that 50uC/mm^2 would be obvious as described above. Optimal thickness of 11 mm is disclosed by Guedon *et al* for DNA based sensor but, however, the optimal thickness for a particular application for other biosensors (such as pyrrole based protein sensor as disclosed by Livache) can be obtain by routine optimization, which can be produced by varying electric current and synthesis time as taught by Guedon *et al* . Protein is considered as an equivalent analyte to DNA by Livache *et al* (se the title for "DNA or peptide array" and section 2.3. wherein "OND or peptide" is recited) and thus one of ordinary skill in the art would also first consider starting with the thickness as described by Guedon *et al* for similarly optimizing the pyrrole-protein thickness of the protein based sensor of Leviche for optimal detection sensitivity.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

With regard to claim 2, Levache *et al* teach that the pyrrole copolymerization process allows the preparation of addressed polypyrrole-DNA/protein on blocks of biosensor array (see section 3.; fig.5 and lines 6-9, right column of page 633) and with regard to claim 3, Livache *et al* teach activating pyrrole through dT10 oligonucleotide linker and coupling to peptides (see section 2.1.).

With regard to claims 10-14, Livache *et al* teach immobilization of biological materials (e.g. peptides, protein) (lines 14-15, right column of page 629) to conductive support to provide biosensors and immobilization of different variation of binding partners on the sensor surface with the expectation of analysis of different analytes would be obvious to one of ordinary skill in the art and one of ordinary skill in the art would expect such

substitution of one binding partner with another to result in an equivalently useful biosensor for analysis of different analytes.

With regard to the polymer film thickness of claims 15-16 and 23-25, as described above, the optimal thickness for a particular application can be obtain by routine optimization, which can be produced by varying electric current and synthesis time as taught by Guedon *et al.*

As for location of the conductive support to biosensor device and use of the biosensor device for different purposes (claims 17-21), Livache's conductive support is meant to be used as biosensors and the location and use of the conductive support constitute obvious variations in parameters which are routinely modified in the art and which have not been described as critical to the practice of the invention.

With regard to claims 26-29, Livache *et al* teach that the copolymerization process is fully compatible with peptide immobilization and their immunodetection, which indicates conservation of activity/ability to bind antibodies by the immobilized protein.

6. Claims 4, 5 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Guedon et al (Anal Chem. 2000) as described above, and further in view of either of Domb *et al* (US 2006/0013850 A1) or Caillat et al (US 6,803,228).

Livache et al in view of Guedon *et al* disclose a method of immobilization of proteins to a conductive support (e.g biochip) by means of a pyrrole

polymer as describes above, but the references fail to disclose pyrrole functionalized with succinimide or maleimide for coupling to protein and ODN.

Domb (US 2006/0013850 A1) discloses coating of electropolymerized pyrrole polymers to conductive support (paragraphs [0019], [0027]). Domb also discloses that the electropolymerized polymer can have a second monomer bearing a reactive group/ functional group (paragraphs [0032], [0044], [0051] and [0055]) for binding to bioactive agents such as proteins, enzymes, nucleic acids (paragraph [0024], [0182], [0243], [0244]). Domb further discloses that activated pyrrole monomers {(e.g. N-alkyl pyrrole derivatives possessing functional groups such as carboxylic acid and derivatives thereof (e.g. acyl halide, ester), amine, hydroxyl, vinyl, acetylene and thiol} can be used for binding bioactive agents (paragraphs [0209], [0396] and example 1, especially scheme 1, scheme 2). Domb *et al* further teach activation of pyrrole with activating agent N-hydroxysuccinimide (see paragraph [0292] for PPA-NHS). Domb et al. further discloses conditions for attachment of bioactive agent such as peptides and proteins to activated pyrrole monomers (paragraph [0396] and [0397]).

Caillat *et al* also disclose pyrrole polymer functionalized with N-hydroxysuccinimide and maleimide for coupling to biomolecules (see 3rd compound from top in column 4 and lines 63-67). Caillat *et al* further teach use of bifunctional crosslinking agent (e.g. comprising N-hydroxysuccinimide ester function and a maleimide function) (column 4, lines 63-67) for activation of pyrrole.

Therefore, given the fact that functionalization of pyrrole with N-hydroxysuccinimide or maleimide is know and common in the art (Domb and Caillat *et al*) for activation of pyrrole for coupling to biomolecules, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to also activate the pyrrole monomer of Livache *et al* with other commonly used activation groups such as succinimide or maleimide with the expectation of similarly producing activated pyrrole useful for producing conductive support containg polymer of pyrrole coupled with protein with a reasonable expectation of success.

With regard to Claims 5 and 22, Domb *et al* and Caillat *et al* teach activation of pyrrole with activating agent such as succinimide and heterobifunctional reagent. Caillat *et al* teach heterobifunctional crosslinking agents comprising maleimido and NHS group and at least one of the heterobifunctioanal group such as GMBS when linked to amine nitrogen of pyrrole or N-ethylamine pyrrole through NHS group of GMBS would provide a linker that would either read or would be obvious to the linkers of claims 5 and 22 absent unexpected results. Since the general conditions for providing activated pyrrole are disclosed in prior art and since as the activating groups that provides linkers of claims 5 and 22 do not seem to be critical to the practice of this invention, the use of commonly known activating group would be obvious to one of ordinary skill in the art for optimization absent unexpected results.

Response to Applicant's argument

7. Applicant's arguments filed 9/14/09 have been fully considered but not persuasive. However, Applicants' amendment necessitated new grounds of rejection under 35 USC 112 first paragraph, as described in this office action.

Applicants argued that in Livache, the peptide is not directly attached to a pyrrole because an additional specific oligonucleotide is interposed between the two molecular moieties, i.e., between the peptide and the pyrrole. This is completely different than the structural configuration required by the invention.

With regard to above argument, it is noted that claim 1 recites coupling "an activated pyrrole monomer" directly to a protein to be attached and the dT_{10} linked pyrrole of Lavache can be regarded as an "activated pyrrore monomer" becasue "activated pyrrole monomer" is not clearly defined in the specification and claim 1 is not limited to a specific "activated pyrrole monomer".

Applicant argued that Guedon is non-analogous art since it refers to DNA and not to protein sensors and also teaches away from the invention should DNA and proteins be improperly equated as similar chemical molecules. Applicants further argued that Guedon, which was applied as a secondary reference in both obviousness rejections, discloses DNA sensors and not protein sensors (see title) and does not suggest or enable the production of the subject matter of the invention which requires attachment of a protein to a conductive support. Applicants further argued that from results of Guedon, one of ordinary skill in the art would have chosen a thickness of more than or

equal to 11 mm, not one with a thickness of 10 mm or less as required by claims 19, 23 and 24. Applicants argued that for a 11 mm thickness, the reflectivity variation is 0.90% and this variation stays above 0.60% for all samples having thicknesses above 11 nm, while it diminishes in a far more important way for samples having thicknesses less than 11 mm (e.g., the reflectivity variation around 0.40% for a sample having a thickness around 9 nm).

The above arguments have been fully considered but are not found persuasive for the reason of records as described in the rejection. DNA and protein are widely known analytes/probes useful for detection/analysis of biomolecules. In various applications oligonucleotide probes can be substituted with a peptide probe for detection of analyte. As for example, expression profile of a cell can be analyzed by detection of mRNA expression or expression of protein and in this case oligonucleotide probes can be substituted with a peptide probe and therefore, Applicants assertion that Guedon is a non-analogous are because the reference deals with DNA sensor instead of protein sensor is not persuasive. The reason that Guedon teaches DNA sensor can not be equated to "teaching away of protein sensor". As described above, DNA and protein probe can be substituted with one another depending on the analytes to be detected and one of ordinary skill in the art would always look for an alternate detection of analytes with the expectation of improving detection sensitivity and reliability of detection. In some cases detection could be more suitable with an oligonucleotide probe,

while in other cases it may be more suitable with a protein probe and thus from the disclosure of DNA sensor of Guedon, one or ordinary skill in the art would be motivated to similarly providing a protein sensor from the knowledge gleaned from Guedon's teaching and the teaching from other related arts.

With regard to thickness of 11 mm, as described above, optimal thickness of 11 mm is disclosed by Guedon *et al* for DNA based sensor but, however, the optimal thickness for a particular application for other biosensors (such as pyrrole based protein sensor as disclosed by Livache) can be obtain by routine optimization, which can be produced by varying electric current and synthesis time as taught by Guedon *et al* . Protein is considered as an equivalent/alternate probe for DNA by Livache *et al* (se the title for "DNA or peptide array" and section 2.3. wherein "OND or peptide" is recited) and thus one of ordinary skill in the art would also first consider starting with the thickness as described by Guedon *et al* for similarly optimizing the pyrrole-protein thickness of the protein based sensor of Leviche for optimal detection sensitivity. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to

be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.) .

With regard to Applicants' argument that for a 11 mm thickness, the reflectivity variation is 0.90% and this variation stays above 0.60% for all samples having thicknesses above 11 nm, while it diminishes in a far more important way for samples having thicknesses less than 11 mm (e.g., the reflectivity variation around 0.40% for a sample having a thickness around 9 nm), the basis for the argument can not be found in the specification.

With regard Domb, Applicants argued that Domb was relied on for teaching reactions between various chemical substrates and pyrroles, but does not suggest the steps required by the present claims or provide a reasonable expectation of success for the superior functionality of proteins attached by these steps. With regard to, Applicants argued that Caillat was cited as teaching a pyrrole polymer functionalized with N-hydroxysuccinimide

and maleimide, but does not suggest the other aspects of the invention or provide a reasonable expectation of success for the superior. With regard to the above argument, it is noted that the rejection is based on combination of references and the Examiner maintains that the combination of the references, as described in the rejection teach the steps required by present claims.

Conclusion

8. Applicants' amendment necessitated new ground(s) of rejection presented in this office action. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicant should point to the page and line numbers of the application corresponding to each amendment, and provide any statements

that might help to identify support for the claimed invention (e.g., if the amendment is not supported in ipsis verbis, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAFIQUL HAQ whose telephone number is (571)272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Primary Examiner, Art Unit 1641